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Use of antimicrobial seal in central venous catheter in hemodialysis patients

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ABSTRACT

Antibiotic lock therapy is an adjunctive therapy used in the treatment of bloodstream infections related to central venous catheters for hemodialysis and consists of the use of high concentrations of ATB to close the lumens between hemodialysis sessions.
The central venous catheter is the least desirable form of vascular access due to its 2- to 3-fold increased risk of morbidity and mortality. Procedures to maintain vascular access can result in inefficient treatments and recurrent hospital admissions, and are constantly a major problem for the healthcare system.
Contamination of the external and internal surface of the central venous catheter by the extraluminal and intraluminal routes, respectively, involves the transfer of microorganisms during manipulation of the central venous catheter, as well as during dressing changes or central venous catheter connection and disconnection.
The purpose of the antimicrobial seal is to prevent colonization and biofilm formation, for which an antimicrobial agent is required. An anticoagulant is needed to prevent catheter dysfunction. This intervention can also be an adjunct to systemic antibiotic therapy and consists of rescuing the catheter by instilling the solution into each lumen of the catheter at the end of each dialysis session for the same duration of systemic therapy, when there is an ongoing bloodstream infection (BSI).

Keywords: Pharmacy Service, Chronic Kidney Disease, Anti-Bacterial Agents, Catheter-Related Infections.

1 INTRODUCTION

Dialysis is defined as the diffusion of molecules in solution through a semipermeable membrane along an electrochemical concentration gradient. In addition to diffusion, solutes can pass through the pores of the membrane through a convective process driven by hydrostatic or osmotic pressure gradients – a process called ultrafiltration. During ultrafiltration, there is no change in solute concentrations, and its primary goal is to remove excess total body water (Himmelfarb & Ikizler, 2010). The dialysis patient population continues to grow. Extrapolation of prevalence data in low- and middle-income countries suggests that the incidence of dialysis initiation appears to be steadily increasing in this group of countries, with further increases expected in the coming decades. In high-income countries, the incidence peaked in the 2000s and has remained stable or slightly decreased since then (Himmelfarb, 2020).

Worldwide, a substantial number of people do not have access to renal replacement therapy (RRT) and millions of people die from kidney failure each year, often without supportive care. In 2010,

2.62 million people received dialysis worldwide and the demand for this therapy is projected to double by 2030. Vascular access-related complications are associated with high rates of hospitalization and infection (McKie, 2022; Lawson, 2020; Luyckx, 2018). According to data from the 2020 Brazilian Dialysis Census, there were 834 active chronic dialysis centers registered in July 2020 with the Brazilian Society of Nephrology (SBN), 3.6% higher than in 2019. The estimated total number of patients was 144,779, which is consistent with the upward trend in the number of dialysis patients (Nerbass, 2022).

The goal of chronic kidney therapy is to slow the progression of chronic kidney disease (CKD) before end-stage renal disease (ESRD) is achieved. CKD is a progressive condition caused by different factors. The solution to slowing the progression of CKD is treatment of all underlying conditions, however, other disorders that affect kidney health require much more extensive treatment (Flagg, 2018). When CKD progresses and kidney function declines to stage five, RRT needs to be considered. RRT includes peritoneal dialysis (PD), hemodialysis (HD), and kidney transplantation (RT). The choice of treatment may involve a shared decision-making model between the patient and health professionals, and is dependent on medical and surgical contraindications, as well as available resources (McKie, 2022; KDIGO, 2012).

Given the increasing prevalence of chronic renal failure and the expectation that hemodialysis will continue to be the mainstay of RRT, at least for the foreseeable future, there is a need to address the current limitations in vascular access for hemodialysis (Lawson, 2020). To start hemodialysis, the first vascular access can be through a central venous catheter (CVC), arteriovenous graft (VAS), or arteriovenous fistula (AVF). Arteriovenous accesses have been recommended by protocols when there is this possibility (Murea, 2019). AVF remains the preferred vascular access over VAS due to its lower infection rate, fewer thrombosis events, and higher long-term patency. CVC is the least desirable form of vascular access due to its 2- to 3-fold increased risk of morbidity and mortality. Procedures to maintain vascular access can result in inefficient treatments and recurrent hospital admissions, and are constantly a major problem for the healthcare system (Vachharajani, 2021).

The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) vascular access guideline suggests that most HD patients starting CVC dialysis should switch to AVF or VAS if possible to reduce the risk of infection/bacteremia, infection-related hospitalizations, and adverse outcomes. Contamination of the outer and inner surface of the CVC by the extraluminal and intraluminal routes, respectively, involves the transfer of microorganisms during the manipulation of the CVC, as well as during dressing change or connection and disconnection of the CVC (KDIGO, 2020). Antimicrobial seal solutions are highly concentrated antiseptic/antibiotic agents or anticoagulants, which are used alone or in combination and are instilled into the tunneled catheters, while the catheter is not in use (Golestaneh, 2018).

The purpose of the antimicrobial seal is to prevent colonization and biofilm formation, for which an antimicrobial agent is required. An anticoagulant is needed to prevent catheter dysfunction. This intervention can also be an adjuvant to systemic antibiotic therapy and consists of rescuing the catheter by instilling the solution into each lumen of the catheter at the end of each dialysis session for the same duration of systemic therapy, when there is an ongoing bloodstream infection (BSI) (Almeida, 2022; Balikci, 2021; Golestaneh, 2018).

2 THEORETICAL FRAMEWORK

Kidney disease is a global public health problem that affects more than 750 million people worldwide. Data collected in recent decades have linked a range of genetic, environmental, sociodemographic, and clinical factors to the risk of kidney disease (Crews, 2019). Kidney failure is a consequence of the progression of acute kidney injury or chronic kidney disease (CKD) causing rapid deterioration of kidney function. CKD is defined by abnormalities in renal structure or function, present for more than 3 months, characterized by a glomerular filtration rate (GFR) below 60 mL/min/1.73 m2 or by the presence of markers of kidney injury, such as albuminuria, urine sediment abnormalities, or electrolyte abnormalities. In end-stage renal disease (ESRD), defined as GFR < 15 mL/min/1.73 m2, patients are at risk of potentially lethal complications without renal replacement therapy (RRT) (KDIGO, 2012). Among these patients, infections are some of the complications that draw the most attention, as they are the second most common cause of hospitalization after cardiovascular diseases (USRDS, 2021).

RRT is a treatment for people with end-stage kidney disease through dialysis or kidney transplantation. The use of dialysis to treat ESRD varies substantially across regions, likely due to differences in population demographics, prevalence of ESRD, and factors affecting access to and supply of RRT (Liyanage, 2015). Dialysis may be used as a temporary short-term measure if the cause of kidney damage is reversible, as a bridge to transplantation, or as definitive treatment in patients unable to undergo transplantation. Regardless of the treatment modality used, the management of kidney disease can have a significant impact on a patient's quality of life (Gupta, 2021).

With the onset of ESRD, about 88% of patients are treated with hemodialysis (HD), and their initial RRT is the first one. Over time, patients may switch to peritoneal dialysis (PD) or receive a transplant. The efficacy of HD is directly related to the quality and consistency of vascular access. More than 80% of patients start HD with central venous catheter (CVC), an unacceptably high rate due to the numerous complications associated with long-term CVC use, including catheter-related infection and death (Gupta, 2021). Arteriovenous fistula (AVF) is widely considered to be the preferred vascular access option for most HD patients, providing the best overall outcomes compared to arteriovenous grafts (VAS) or CVC (Thurlow, 2021).

The Brazilian reality regarding dialysis, according to the census conducted in 2020, in relation to vascular access, 25% of HD patients used CVC. There was a decrease in the use of short-term catheters and prostheses, while the use of long-term catheters increased (11%). HD continued to be the treatment for most patients (92.6%) and 7.4% were treated with PD. The treatment was financed by the public health system for 81.6% of the patients and by the private health plan for 18.4% of the patients in the participating units (Nerbass, 2022).

CVCs are used to provide vascular access for both short-term and long-term use. Non-tunneled CVCs are typically for short-term hospital use. Long-acting (tunneled) CVCs are placed under the skin and into the internal jugular vein (most commonly, due to its easy accessibility and path), from where they pass through the brachiocephalic vein and superior vena cava before terminating in the right atrium. Long-term catheter use is often a concern due to the numerous complications associated with this approach, the most common being infection, which can be located in the catheter or occur in the bloodstream (Agarwal, 2019; Lawson, 2020).

In addition, the use of CVC is associated with higher rates of all-cause mortality, fatal infection, and cardiovascular events than the use of fistulas or arteriovenous grafts (Lawson, 2020). Central vein stenosis or occlusion is often found in patients undergoing HD due to prolonged CVC use, multiple CVC insertions, thrombosis, and catheter-related bloodstream infection. Total occlusion of the central vein prevents the insertion of any form of vascular access into the upper extremity. Options are limited to a lower extremity CVC or arteriovenous access to maintain HD treatment (Vachharajani, 2021). Other CVC-related complications can be hemorrhage, pneumothorax, arterial puncture, and catheter dysfunctions such as low blood flow rates and inadequate flow (Balikci, 2021).

Catheters have constantly evolved to minimize complication rates, improve catheter patency, optimize blood flow, minimize intraluminal thrombosis, increase biocompatibility, and decrease the rate of catheter infection, twisting, collapse, or rupture (El Khudari, 2022). The management of CVC infections is complex and can be influenced by the type of device, microbial etiology, and clinical conditions of the patient. The 2009 Infectious Diseases Society of America (IDSA) guidelines recommend catheter removal in certain situations. However, catheter removal is not always feasible in children, especially younger children or those with genetic conditions, when alternative venous approaches may be difficult to establish in a short time to ensure continuity of intravenous infusions (Buonsenso, 2022). After insertion, the catheter often requires repeated interventions to maintain its usefulness. In fact, the rates of primary patency failure and catheter removal in the first year are estimated to be 91% and 52%, respectively (Lawson, 2020).

Infection is the most common long-term complication associated with hemodialysis catheter use. For most catheter patients, the question is when an infection will occur. As the number of catheter days increases, the likelihood of bacteremia increases. Risk factors include older age, diabetes,

malnutrition, frequent catheter manipulation, longer duration of catheter use, bacterial colonization, and contamination of the dialysis solution (El Khudari, 2022). Approximately three-quarters of the pathogenic microorganisms that cause infection are gram-positive and one-quarter are gram-negative bacteria. Systemic antibiotic therapy and the use of antimicrobial seals are the current treatment approaches and are not fully effective. When the infection originates from the extraluminal space of the catheter, blood from the catheter lumen does not indicate infection in the culture, and antimicrobial seal therapy will not be sufficient to terminate the catheter-related infection (CRF). CRF is basically the presence of a certain number of organisms in the catheter segment with clinically existing bacteremia or a local infection that may or may not be accompanied by bloodstream infection (Balikci, 2021).

The use of antibiotic solutions to fill the catheter lumen can be used as a complementary treatment to systemic antibiotic therapy when there is a catheter-related bloodstream infection. However, there are no robust randomized controlled trials proving the favorable effect of such solutions, but there are observational studies showing that the application of intraluminal antibiotic solutions together with a systemic antibiotic leads to the eradication of bacteria and reduces the need for replacement or removal of the tunneled catheter (Borisov & Linkova, 2020). A systematic review demonstrated that in the meta-analysis of a subgroup with an antibiotic + heparin seal (5 studies) or antibiotic + citrate (3 studies) compared with a heparin seal alone, there was a statistically significant reduction in catheter-related bloodstream infection in patients undergoing haemodialysis. However, the authors concluded that the included studies have some shortcomings and may have introduced biases. The results should be interpreted with caution due to the small number of studies (Snaterse, 2010).

The definition of the diagnostic criteria of infection for the epidemiological surveillance of healthcare-associated infections (HAIs) in health services allows the necessary congruence to identify the case, collect and interpret the information in a systematic manner by health system professionals and managers. In 2010, with the objective of standardizing the epidemiological criteria of HAI at the national level, Anvisa's Health Services Surveillance and Monitoring Management (GVIMS/GGTES/Anvisa) published the Manual for Diagnostic Criteria for Healthcare-Associated Infection. For the preparation of this manual, technical groups (WG) were formed with specialists from all over the country. The WGs were also responsible for the revisions of the manual in 2016, 2019 and 2021 (ANVISA, 2010; ANVISA, 2021).

One of the indicators that must be reported nationally is known as Primary Bloodstream Infection (IPCS). The diagnostic criteria for HAIs associated with invasive devices, of mandatory notification, can be checked in Annex I, according to Technical Note GVIMS/GGTES No. 07/2021,

which informs how the mandatory national notification for the year 2022 for the National Health Surveillance Agency (ANVISA) should be (ANVISA, 2021).

IPCS is the presence of one or more microorganisms in the bloodstream, whose origin is not related to any other focus of infection (primary focus), as defined in the national diagnostic criteria. In this sense, the primary focus is the bloodstream itself, which is why the infection is called IPCS (ANVISA, 2021). Laboratory-confirmed primary bloodstream infection (SLBI) is defined as infection in a patient using a central line for a period longer than two consecutive days (from D3 onwards, with the day of insertion being considered D1, regardless of the time of insertion) and that on the date of infection the patient was using the device or it had been removed on the previous day (ANVISA, 2021).

A central catheter is defined by the presence of an intravascular device used for infusion, blood sample collection, or hemodynamic monitoring, whose termination is positioned close to the heart or in a large vessel. The following are considered large vessels: aorta, pulmonary artery, vena cavae, brachycephalic veins, internal jugular veins, subclavian veins, external and common iliac veins, femoral veins, and in newborns all venous or arterial umbilical catheter (ANVISA, 2021). Among the types of central catheters for epidemiological surveillance purposes are tunneled permanent central catheters (which include tunneled hemodialysis catheters) and temporary non-tunneled central catheters (which include non-tunneled hemodialysis catheters) (ANVISA, 2021).

REFERENCES

Himmelfarb, Jonathan, and T. Alp Ikizler. Hemodialysis. *New England Journal of Medicine* 363.19 (2010): 1833-1845. https://doi.org/10.1056/NEJMra0902710

Himmelfarb, J., Vanholder, R., Mehrotra, R. *et al.* The current and future landscape of dialysis. *Nat Rev Nephrol* 16, 573–585 (2020). https://doi.org/10.1038/s41581-020-0315-4

McKie, Amanda L., Murray Turner, and Catherine Paterson. "What are the qualitative experiences of people affected by kidney failure receiving haemodialysis?." *Journal of Renal Care* (2022). https://doi.org/10.1111/jorc.12442

Lawson, J.H., Niklason, L.E. & Roy-Chaudhury, P. Challenges and novel therapies for vascular access in haemodialysis. *Nat Rev Nephrol* 16, 586–602 (2020). https://doi.org/10.1038/s41581-020-0333-2

Luyckx, Valerie A., Marcello Tonelli, and John W. Stanifer. The global burden of kidney disease and the sustainable development goals. Bulletin of the World Health Organization 96.6 (2018): 414. https://doi.org/10.2471/BLT.17.206441

Nerbass, Fabiana B. *et al.* Brazilian Dialysis Survey 2020. *Brazilian Journal of Nephrology* (2022). https://doi.org/10.1590/2175-8239-JBN-2021-0198

Flagg, Amanda J. Chronic renal therapy. *Nursing Clinics* 53.4 (2018): 511-519. https://doi.org/10.1016/j.cnur.2018.07.002

Kidney Disease: Improving Global Outcomes, and CKD Work Group. "KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease." Kidney Int 3.1 (2013): 1-150.

Murea, Mariana, et al. Vascular access for hemodialysis: A perpetual challenge. *Seminars in dialysis*. Vol. 32. No. 6. 2019. https://doi.org/10.1111/sdi.12828

Vachharajani, Tushar J., Jonathan J. Taliercio, and Evamaria Anvari. "New devices and technologies for hemodialysis vascular access: a review." *American Journal of Kidney Diseases* 78.1 (2021): 116-124. https://doi.org/10.1053/j.ajkd.2020.11.027

Lok CE, Huber TS, Lee T, et al; KDOQI Vascular Access Guideline Work Group. KDOQI clinical practice guideline for vascular access: 2019 update. Am J Kidney Dis. 2020;75(4)(suppl 2):S1-S164.

Golestaneh, Ladan, and Michele H. Mokrzycki. Prevention of hemodialysis catheter infections: Ointments, dressings, locks, and catheter hub devices. *Hemodialysis International* 22.S2 (2018): S75-S82. https://doi.org/10.1111/hdi.12703

Crews, D.C., Bello, A.K., Saadi, G. *et al.* Burden, access, and disparities in kidney disease. *J Nephrol* 32, 1–8 (2019). https://doi.org/10.1007/s40620-019-00590-6

United States Renal Data System. *2020 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States*. https://adr.usrds.org/2020 (2021).

Liyanage, Thaminda, et al. "Worldwide access to treatment for end-stage kidney disease: a systematic review." *The Lancet* 385.9981 (2015): 1975-1982. doi: 10.1016/S0140-6736(14)61601-9

Gupta, Ryan, Karen Woo, and A. Yi Jeniann. "Epidemiology of end-stage kidney disease." *Seminars in vascular surgery*. Vol. 34. No. 1. WB Saunders, 2021. doi: 10.1053/j.semvascsurg.2021.02.010

Thurlow, John S., et al. "Global epidemiology of end-stage kidney disease and disparities in kidney replacement therapy." *American journal of nephrology* 52.2 (2021): 98-107. doi: 10.1159/000514550

Almeida BM, Moreno DH, Vasconcelos V, Cacione DG. Interventions for treating catheter-related bloodstream infections in people receiving maintenance haemodialysis. Cochrane Database of Systematic Reviews 2022, Issue 4. Art. No.: CD013554. https://doi.org/10.1002/14651858.CD013554.pub2

Balikci, Elif, *et al.* Surface modification strategies for hemodialysis catheters to prevent catheter-related infections: A review. Journal of Biomedical Materials Research Part B: Applied Biomaterials 109.3 (2021): 314-327. https://doi.org/10.1002/jbm.b.34701

Agarwal, Anil K., Nabil Haddad, and Khaled Boubes. "Avoiding problems in tunneled dialysis catheter placement." *Seminars in dialysis*. Vol. 32. No. 6. (2019) https://doi.org/10.1111/sdi.12845

El Khudari, Husameddin, et al. "Hemodialysis Catheters: Update on Types, Outcomes, Designs and Complications." *Seminars in Interventional Radiology*. Vol. 39. No. 01. Thieme Medical Publishers, Inc., 2022. https://doi.org/10.1055/s-0042-1742346

Buonsenso, Danilo, et al. "Catheter salvage strategies in children with central venous catheter related or associated bloodstream infections: a systematic review and meta-analysis." *Journal of Hospital Infection* (2022). https://doi.org/10.1016/j.jhin.2022.03.010

Borisov, Biser, and Stela Linkova. "Infectious Complications of Hemodialysis Tunneled Catheters — Types, Diagnosis, and Treatment Strategies." *Indian Journal of Surgery* 82.4 (2020): 460-464.

Snaterse, M., et al. "Antibiotic-based catheter lock solutions for prevention of catheter-related bloodstream infection: a systematic review of randomised controlled trials." *Journal of Hospital Infection* 75.1 (2010): 1-11.

ANVISA. Critérios Diagnósticos de Infecções Relacionadas à Assistência à Saúde. Agência Nacional de Vigilância Sanitária. (2017) Disponível em: <https://bvsms.saude.gov.br/bvs/publicacoes/criterios_diagnosticos_infeccoes_assistencia_saude.pdf > Acesso em: 7 out. 2022.

ANVISA. Nota Técnica GVIMS/GGTES N° 07/2021 - Critérios Diagnósticos das Infecções Relacionadas à Assistência à Saúde (IRAS): notificação nacional obrigatória para o ano de 2022. Agência Nacional de Vigilância Sanitária. (2021) Disponível em: <https://www.gov.br/anvisa/pt-br/centraisdeconteudo/publicacoes/servicosdesaude/notas-tecnicas/2021/nota-tecnica-gvims-ggtes-no-07-2021-criterios-diagnosticos-das-infeccoes-relacionadas-a-assistencia-a-saude-iras-notificacao-nacional-obrigatoria-para-o-ano-de-2022> Acesso em: 7 out. 2022.

ATTACHMENT

ANNEX I

TECHNICAL NOTE GVIMS/GGTES Nº 07/2021 Diagnostic criteria for Healthcare-Associated Infections (HAI): mandatory national notification for the year 2022

Diagnostic criteria for HAIs associated with invasive devices, which must be notified:

1. Diagnostic Criteria for Primary Central Line-Associated Bloodstream Infection

1.1 Diagnostic Criteria for Central Line-Associated Laboratory-Confirmed Primary Bloodstream Infection (IPCSL) in Adult and Pediatric Patients

Criterion 1: Central line-associated IPCSL caused by pathogenic microorganism in adults and children > 28 days
Patient > 28 days in use of a central catheter for a period longer than two consecutive days (D1 being the day of device installation) and that on the date of infection the patient was using the device or it was removed the day before. **And** It has a bacterial or fungal pathogenic microorganism, not included in the list of commensal microorganisms1, isolated in a blood sample2: 1. Identified from one or more blood samples obtained in blood culture **OR** 2. Identified genus and species, or at least genus, by validated methods of non-culture-based microbiological testing[3] **And** The microorganism identified is not related to another infectious focus4
Notes
1The complete list of skin contaminating microorganisms (commensals) can be consulted at the link: https://www.gov.br/anvisa/pt br/centralsofcontent/publications/health services/publications/list-of-common diners.xlsx 2The collection of blood samples should preferably be done by peripheral puncture, but it is accepted that the IPCSL caused by a pathogenic microorganism is defined using the results of blood culture or a microbiological test not based on culture of samples collected from a central line, in cases where it is not possible to perform peripheral collection. 3Non-culture-based microbiological tests are molecular, automated tests performed from blood samples. These tests can use, for example, multiplex PCR, miniaturized magnetic resonance imaging technology or DNA sequencing of microbial cells for microbiological diagnosis. It is worth emphasizing that if the blood culture was collected 2 days before or 1 day after the non-culture-based microbiological test, we should consider the result of the blood culture (gold standard) for the surveillance of IPCSL and disregard the result of the non-culture-based microbiological test. 4If the microorganism is related to another infectious source (as per Annex 1 of this document), this bloodstream infection will not be primary, and therefore should not be reported as IPCSL.
Criterion 2: Central line-associated IPCSL caused by skin-contaminating microorganism in adults and children > 1 year
Patient > 1 year in use of a central catheter for a period longer than two consecutive days (D1 being the day of device installation) and that on the date of infection the patient was using the device or it was removed on the previous day **And**

Have at least one of the following signs or symptoms:
o Fever (>38°C)
o Chills
o Hypotension (systolic pressure ≤ 90 mmHg in adults and children, see clinical parameters by age group in Annex l of the HAI Diagnostic Criteria manual)
And
It has skin-contaminating microorganisms (commensals1a,1b), for example: *Corynebacterium* spp. (excludes C. diphtheriae), *Bacillus* spp. *(*excludes *B. anthracis), Propionibacterium spp.,* coagulase-negative *Staphylococcus,* Viridans group Streptococcus, Aerococcus *spp.* and *Micrococcus* spp, identified in TWO or more blood cultures, collected at different times, on the same day or at most on the following day2,3.
And
The microorganism identified is not related to another infectious focus4
And
The signs/symptoms and the result of the blood culture occurred in the window period of infection.

Criterion 3: Central line-associated IPCSL caused by skin-contaminating microorganism in children > 28 days and ≤ 1 year

Patient > 28 days and 1 year ≤ using a central catheter for a period longer than two consecutive days (D1 being the day of device installation) and that on the date of infection the patient was using the device or it was removed on the previous day
And
Patient has at least one of the following signs or symptoms:
o Fever (>38°C)
o Hypothermia (<35°C)
o Apnea
o Bradycardia (see clinical parameters by age group in Appendix l of the HAI Diagnostic Criteria manual)
And
It has skin-contaminating microorganisms (commensals1a,1b), for example: *Corynebacterium* spp. (excludes C. diphtheriae), *Bacillus* spp. *(excludes B. anthracis), Propionibacterium spp.,* coagulase-negative Staphylococcus, Viridans group Streptococcus, Aerococcus *spp.* and *Micrococcus* spp, identified in TWO more blood cultures, collected at different times, on the same day or at most on the following day2,3.
And
The microorganism identified is not related to another infectious focus4
And
The signs/symptoms and the result of the blood culture occurred in the window period of infection.

Notes (criterion 2 and 3)

1aThe complete list of skin contaminating microorganisms (commensals) can be consulted at the link: https://www.gov.br/anvisa/pt br/centralisdeconteúdo/publications/servicosdesaude/publicacoes/llista-de-commensals comums.xlsx
1bThe two corresponding skin contaminant (commensal) samples represent a single element for fulfillment of criterion 2 or 3 and the date of collection of the first sample is used to determine the date of infection.
2The phrase "two or more blood cultures collected at different times" means that:
At least two separate blood sample collections were performed on the same day or on consecutive days, with individualized preparation (skin antisepsis or connector disinfection steps) from each collection site/site during collection.
The purpose of this is to ensure that preparation/antisepsis is carried out at the collection site/site for each collection carried out. In this way, the risk of contamination of the collection being considered IPCSL is reduced.
For example: Prepare individually, i.e., perform the antisepsis/disinfection steps separately in:
- two blood collections from different sites (different peripheral venipunctures, the combination of a venipuncture and collection of a lumen from the central line, or collection of two different lumens from the same central catheter {each lumen must be prepared individually before collection, remembering that this type of collection is allowed in case of exception when it is not possible to perform peripheral collection})

OR

- two blood collections from the same site (collected at different times)

3The collection of blood samples for blood cultures should preferably be done by peripheral vein puncture, because samples collected from the catheter have a high risk of contamination by commensal microorganisms and, therefore, a greater chance of false-positive results, so positive blood cultures collected only from the central line should be avoided. However, in exceptional situations, it is accepted that SLBI caused by a skin

contaminating agent is defined using two positive blood cultures collected from a central line, in cases where peripheral collection is not possible. The need for adequate preparation of the blood collection site/site is reinforced (see details of blood culture collection in the annex to the chapter on bloodstream infection of the Manual of Diagnostic Criteria for HAIs).
4If the microorganism is related to another infectious source (as per Annex 1 of this document), this bloodstream infection will not be primary, and therefore should not be reported as IPCSL.